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THE ACUTE TOXICITY OF CHLORINE PENTAFLUORIDE

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13. ABSTRACT

This report was presented at the Proceedings of the 2nd Annual Conference on Environmental Toxicology, sponsored by the SysteMed Corporation and held in Fairborn, Ohio on 31 August, 1 and 2 September 1971. Major technical areas discussed included toxicological evaluation of volatile halogenated compounds, protection of the public against air pollution and toxicological problems with aircraft, missiles, and space vehicles.

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PAPER NO. 21

THE ACUTE TOXICITY OF CHLORINE PENTAFLUORIDE

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INTRODUCTION

Chlorine pentafluoride (ClF_5) is one of a series of reactive fluorinated oxidizing agents of interest to the Air Force as a potential oxidizing propellant for missiles. As you might suspect from its very name, this is an unusual chemical species, and it may only be formed under extreme conditions of temperature and pressure. Its existence was first reported only eight years ago by Smith (1963) who described the molecule as having a square pyramidal structure as shown in figure 1. The chlorine atom lies almost in the same plane as the four fluorine atoms which comprise the base of this pyramid. The figure shows the outline of the shape of the molecule, and the bonds go directly from the chlorine atom to each of the fluorine atoms at the extremities of the molecule.

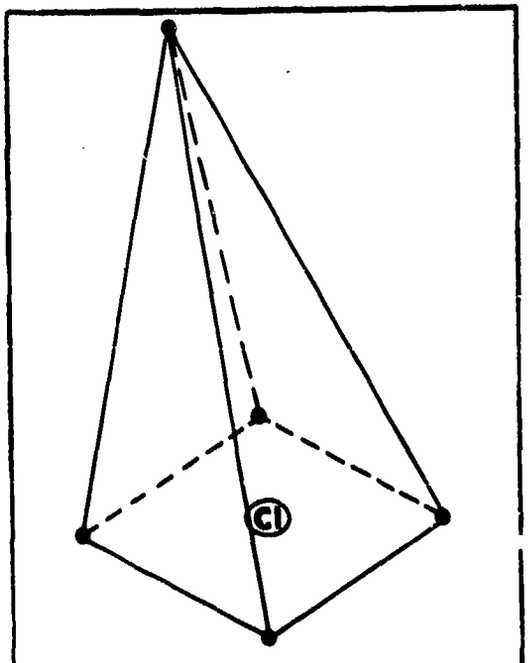

Figure 1. GEOMETRIC CONFIGURATION OF ClF_5 MOLECULE

Begin

Little is known about its physical chemical properties, such as exactly which reactions it will enter into, how quickly it reacts, and exactly what products result from its reaction with different compounds. As an example, the proposed reaction for ClF_5 with water is this:

$$ClF_5 + 2H_2O \longrightarrow ClO_2F + 4HF$$

Smith (1963), who first made the molecule, claims that this reaction occurs slowly if at all. Dost and Wang (1970) reported that the reaction did occur, and that it was a slow reaction. Pilipovich et al. (1967), however, reported that ClF_5 reacts violently with water in any form.

Very little investigation of the acute inhalation toxicity of ClF_5 has been reported. Weinberg and Goldhamer (1967) described two 10-minute exposures of rats:

400 ppm	10 minutes	6/6 dead
200 ppm	10 minutes	1/10 dead

A periodic sacrifice of the nine survivors from the 200 ppm exposure over the 24 hours following exposure showed evidence of a reversible alveolar destruction.

The present study was undertaken to obtain symptomatic and pathological information resulting from acute exposure to ClF_5 gas, and to determine the LC_{50} values for exposure of rats, mice, dogs, and monkeys for 15, 30, and 60 minutes.

METHODS

To reduce the hazard associated with use of full-strength ClF_5, concentrated ClF_5 was diluted in dry nitrogen and supplied in dilution tanks having a concentration of about 1.5%. These dilutions were carried out at our oxidizer dilution facility, which was described at last year's conference by Mr. Erk (Erk and Kaczmarek, 1970). The ClF_5 was introduced into the exposure chamber by metering it through a corrosion resistant gas regulator and a Fischer-Porter flow meter.

All exposures were made in a modified Rochester chamber under ambient conditions (Haun et al., 1969). Exposures were routinely conducted at a chamber flow rate of 70 cfm at a slight negative pressure, with relative humidity of about 50%, although this was somewhat variable depending upon ambient relative humidity conditions. Exposure groups consisted of 10 rats, 10 mice, 4 dogs, or 4 monkeys. Male Sprague-Dawley rats, male ICR mice, male and female beagle dogs, and male and female rhesus monkeys were the experimental animals used in this study.

Contaminant concentrations within the chamber were monitored continuously during all exposures. Analytical determinations were made with a fluoride ion specific electrode which was calibrated with bag samples having known concentrations of ClF_5 in air. The analysis was capable of detecting 10 to 1000 ppm ClF_5.

The animals were observed for visible symptoms and mortality both during exposure and for a 14-day postexposure observation period. Gross and histopathological examinations of a representative sample of each of the four species for each exposure time were made.

RESULTS

There are no accounts in the literature of the symptomatology of ClF_5 exposure, but, as might be expected, symptoms appear to be similar to those caused by HF, OF_2, and ClF_3. Rodents showed lacrimation, rhinorrhea, salivation, and respiratory distress during exposure. This generally led to anoxic hyperactivity just prior to death, a state which very closely resembled CNS stimulation.

Dogs and monkeys showed unmistakable signs of irritation almost immediately after onset of the exposure. This was evidenced by marked salivation, lacrimation, and sneezing, which progressed to nausea, dyspnea, and, in some cases, unconsciousness prior to the end of the exposure, with both dogs and monkeys. Cyanosis was usually evident by the end of the exposure with both dogs and monkeys. The severity and progression of these symptoms was in general directly related to increasing concentration and duration of exposure. Corneal opacity was a common occurrence with all species, but was less pronounced in the monkeys, possibly due to the fact that their eyes were kept closed during exposure to a greater extent than the other species.

The death pattern appeared similar to that of OF_2, HF, and ClF_3, with delayed deaths being found in all four species. Dogs and monkeys generally died within 48 hours following exposure, and rodent deaths tended to occur throughout the entire 14-day postexposure period. There were more delayed deaths with mice than with rats.

Gross pathological examination of animals that died either during or after exposure showed that the lungs and respiratory passages were the primary targets for ClF_5 damage. Animals of all four species that died during exposure exhibited similar pathology. The lungs failed to collapse upon opening the chest cavity, and were found to contain edema fluid and blood, indicating alveolar destruction. Nasal and bronchial passages generally contained large amounts of mucus and other fluids, and, in some cases, blood. There were no other apparent systemic effects.

Tissue samples have been taken for histopathological examination, but these have not yet been processed. Examination of animals surviving the full 14-day postexposure observation period showed that the effects on the respiratory system were almost completely reversible within this period of time.

The mortality data and LC_m values with their 95% confidence limits are presented in the next four tables. Also included in these tables is a record of times to death for all species tested. You will notice that the 15-minute rat data (table I) is very similar to the 10-minute data reported by Weinberg and Goldhamer (1967).

TABLE I

ClF_5 ACUTE TOXICITY RESULTS

RATS

Duration (minutes)	Average Conc. (ppm)	Conc. Range (ppm)	Mortality Response	Postexposure Time to Death Hours (no. dead)	Days (no. dead)
15	175	145-194	1/10		6 (1)
15	235	195-249	4/10	3.5 (1), 17.5 (2)	12 (1)
15	258	210-317	6/10 1*	12 (2), 14 (2)	13 (1)
15	300	251-318	7/10 1*	24 (2)	7 (1), 8 (1), 9 (1), 11 (1)
15	325	300-349	9/10 3*	24 (3)	6 (1), 8 (2)
15	373	339-384	6/10 3*	24 (3)	
15	432	400-442	9/10 8*	24 (1)	
		15 min. LC_{50}: 257 (210-314)			
30	120	95-125	0/10		
30	163	140-175	0/10		
30	185	162-200	3/10 3*		
30	190	138-213	6/10 3*	48 (1)	7 (1), 9 (1)
30	233	201-253	9/10 5*	24 (1)	5 (1), 12 (1), 14 (1)
30	250	200-270	10/10 10*		
		30 min. LC_{50}: 194 (135-278)			
60	80	55- 86	0/10		
60	100	77-107	1/10 1*		
60	120	102-128	4/10 3*	[illegible]	
60	136	112-156	8/10 6*	8 (2)	
		60 min. LC_{50}: 122 (108-139)			

*Deaths occurred during exposure

TABLE II

ClF_5 ACUTE TOXICITY RESULTS

MICE

Duration (minutes)	Average Conc. (ppm)	Conc. Range (ppm)	Mortality Response	Postexposure Time to Death Hours (no. dead)	Days (no. dead)
15	100	81-112	2/10		8 (1), 12 (1)
15	130	100-145	4/10		8 (1), 9 (1), 10 (1), 11 (1)
15	166	128-181	7/10		7 (2), 9 (5)
15	174	150-188	7/10 1*		9 (1), 11 (2), 12 (2), 14 (1)
15	195	175-203	6/10	2.5 (1)	7 (2), 8 (2), 12 (1)
15	212	165-230	9/10 3*	8 (1)	5 (1), 7 (1), 8 (1), 9 (1), 12 (1)
15	231	175-246	8/10 1*	.5 (1), 17 (1)	6 (2), 7 (1), 8 (1), 10 (1)
15	305	260-320	9/10 6*	1 (2), 19 (1)	
15	360	315-387	15/15 15*		
		15 min. LC_{50} : 144 (112-186)			
30	70	83- 50	2/10	5 (1), 48 (1)	
30	90	73-124	3/10	20 min. (3)	
30	117	90-138	6/10 3*	5 min. (2), 14 (1)	
30	120	102-141	5/10 3*	1.5 (1), 4.5 (1)	
30	140	93-163	8/10	5 min. (2), 5 (1), 6 (1), 7 (1), 1 (1), 24 (1)	7 (1)
30	145	116-163	8/10 4*	4.5 (1), 8 (1)	9 (1), 11 (1)
30	166	112-180	9/10	5 min. (5), 1 (1), 14 (1)	8 (1), 11 (1)
30	175	152-183	10/10 7*	15 (1)	6 (1), 12 (1)
		30 min. LC_{50} : 105 (93-119)			
60	35	22- 40	1/10	6 (1)	
60	47	35- 73	2/10 2*		
60	62	30- 68	5/10 1*	5 min. (1), 2 (1), 9 (2)	
60	75	45- 82	9/10 5*	6 (1), 9 (1), 10 (1), 12 (1)	
		60 min. LC_{50} : 57 (47-70)			

*Deaths occurred during exposure

TABLE III

ClF_5 ACUTE TOXICITY RESULTS

DOGS

Duration (minutes)	Average Conc. (ppm)	Conc. Range (ppm)	Mortality Response	Postexposure Time to Death Hours (no. dead)	Days (no. dead)
15	168	130-185	0/4		
15	202	130-327	1/4	18 (1)	
15	300	206-352	2/4	5 (1), 21.5 (1)	
15	360	332-402	2/4	10 (1), 17 (1)	
15	443	403-460	4/4	17 (1), 21 (1), 30 (2)	
15 min. LC_{50}: 298 (238-374)					
30	102	89-113	1/4	29 (1)	
30	150	110-187	1/4	16.5 (1), 26 (1)	
30	190	138-213	2/4	20.5 (1), 29.5 (1)	
30	223	185-275	3/4	1 (1), 17 (1), 19 (1)	
30	252	155-307	3/4	10 (1), 21 (1), 39 (1)	
30	274	209-345	4/4	2.5 (1), 10 (1), 12 (1), 13 (1)	
30 min. LC_{50}: 156 (113-215)					
60	63	57- 75	0/4		
60	110	61-125	1/4	23 (1)	
60	128	65-182	2/4	15 (1), 35 (1)	
60	143	110-154	4/4	22 (1), 37 (1)	6 (1), 10 (1)
60	170	130-175	4/4	75 (1), 14 (1), 15 (1), 24 (1)	
60 min. LC_{50}: 122 (111-134)					

TABLE IV

ClF_5 ACUTE TOXICITY RESULTS

MONKEYS

Duration (minutes)	Average Conc. (ppm)	Conc. Range (ppm)	Mortality Response		Postexposure Time to Death Hours (no. dead)	Days (no. dead)
15	165	152-175	0/4			
15	193	160-210	1/4		16 (1)	
15	225	185-265	3/4		12 (1), 24 (1)	3 (1)
15	335	300-355	3/4		2 (1), 4 (1), 6 (1)	
15	395	285-490	3/4		3 min. (1), 2 (1), 4 (1)	
		15 min. LC_m : 249 (191-326)				
30	198	127-225	0/4			
30	218	168-262	2/4	1*	30 min. (1)	
30	236	195-255	4/4		5 min. (1), 1 (2), 2.5 (1)	
		30 min. ALC_m : 218				
60	116	68-135	0/4			
60	122	102-140	1/4		9 (1)	
60	140	87-155	1/4		3 (1)	
60	189	112-212	2/4	2*		
60	215	160-230	2/4		5 min. (1), 15 min. (1)	
60	223	166-252	4/4	1*	5 min. (2), 35 (1)	
		60 min. LC_m : 173 (148-204)				

*Deaths occurred during exposure

Table V is a summary of the LC_{50} data for each of the four species that were studied, and for each of the three exposure time limits used.

TABLE V

SUMMARY OF ACUTE ClF_5 TOXICITY LC_{50} VALUES

Species	LC_{50} Values in ppm 15 min.	30 min.	60 min.
Rats	257	194	122
Mice	144	105	57
Dogs	298	156	122
Monkeys	249	218	173

The CT (concentration x time) values for each of the ClF_5 LC_{50} values are presented in table VI.

TABLE VI

CT VALUES FOR ClF_5 ACUTE TOXICITY

Species	Exposure Time 15 min	30 min.	60 min.
Rats	3855	5820	7320
Mice	2160	3150	3420
Dogs	4470	4680	7320
Monkeys	3750	6540	10380

As you may have noticed in looking at the individual data, the theoretical CT relationship does not exist for ClF_5. For some of the data, the 30- and 60-minute mouse data and the 15- and 30-minute dog data, it holds very well; but it does not hold true for any single species, or for any particular time limits. The reason for this probably lies in the nature of the ClF_5 itself. As I stressed earlier, very little is known about how this compound reacts, and it is quite probable that different reactions and

different reaction rates occur under different conditions of temperature, relative humidity, and at either high or low concentrations of ClF_5. The absence of a CT relationship is probably due to the presence of varying amounts of ClF_5 breakdown products in the chamber, with each of them having some effect on the overall toxicity that we observed. Since our analysis could only measure total concentration of fluoride ions in the chamber, it was impossible to determine what specific fluorine-containing compounds were present, and in what amounts they existed.

In summary, I would like to compare the results of the 60-minute ClF_5 exposures to 60-minute data for OF_2, ClF_3, and HF. The data from these compounds were also obtained in our laboratory, so the methods involved in gathering all of these comparative data were essentially identical. These data are presented in table VII.

TABLE VII

COMPARATIVE 60-MINUTE TOXICITY DATA
FOR FLUORINATED OXIDIZERS AND HF
(in ppm)

Species	OF_2	ClF_5	ClF_3	HF
Rats	2.6	122	299	1276
Mice	1.5	57	178	501
Dogs	26.0	122	---	---
Monkeys	26.0	173	230	1774

Probably the most obvious and the most interesting comparison is that of ClF_5 with HF. In every case in which the two compounds may be compared, the ClF_5 was almost exactly 10 times more toxic than HF. ClF_5 was also two to three times more toxic than ClF_3, but was far less potent than OF_2. Another interesting point is that, with the exception of monkeys, ClF_3 is about three times more toxic than HF, but ClF_5 is about 10 times more toxic than HF, so the toxicity of ClF_5 cannot be directly explained by a simple breakdown of ClF_5 to HF.

SUMMARY

The acute toxicity of exposure of rats, mice, dogs, and monkeys to the fluorinated oxidizer chlorine pentafluoride (ClF_5) for 15, 30, and 60 minutes has been studied. The LC_{50} values, with 95% confidence limits, for each species and each chosen time were presented. Associated pathology resulting from these exposures

was discussed. The toxicity data for ClF_3 were compared to two other fluorinated oxidizers (ClF_3 and OF_2) and to HF. ClF_3 was found to be far less toxic than OF_2, about two to three times more toxic than ClF_3, and almost exactly 10 times more toxic than HF.

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